

SHEET 1 OF 7

Form PTO - 1449 (Modified)

FORM PTO-1449 U.S. DEPARTMENT OF COMMERCE
(Modified) PATENT AND TRADEMARK OFFICE

ATTY. DOCKET NO.
4952.US.C1

SERIAL NO.
09/735,056

INFORMATION DISCLOSURE
STATEMENT BY APPLICANT

(Use several sheets if necessary)

APPLICANT(S)

L. Katz, et al.

FILING DATE

December 11, 2000

GROUP

1652

(37 CFR 1.98 (b))

U.S. PATENT DOCUMENTS

EXAMINER INITIAL	PATENT NUMBER	ISSUE DATE	INVENTOR	CLASS	SUB CLASS	FILING DATE
WWM	A1 4,874,748	10-17-89	Katz, et al.	514	29	
WWM	A2 4,921,801	05-01-90	Rao, et al.	435	474	
WWM	A3 4,935,340	06-19-90	Baltz, et al.	435	6	
WWM	A4 5,081,023	01-14-92	Yaginuma, et al.	435	76	
WWM	A5 5,087,563	02-11-92	Beremand, et al.	435	69.7	
WWM	A6 5,110,728	05-05-92	Kridl, et al.	435	69.1	

FOREIGN PATENT OR PUBLISHED FOREIGN PATENT APPLICATION

	DOCUMENT NUMBER	PUBLICATION DATE	COUNTRY OR PATENT OFFICE	CLASS	SUB CLASS	TRANSLATION	
						YES	NO
WWM	B1 EP 0 204 549 A2	12-10-86	EPO				
WWM	B2 EP 0 238 323 A2	09-23-87	EPO				
WWM	B3 WO 93/13663	06-22-93	WIPO				
WWM	B4 WO 96/40968	12-19-96	WIPO				

OTHER DOCUMENTS (Including Author, Title, Date, Place of Publication)

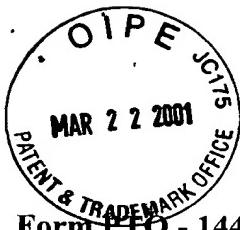
WWM	C1	Aigle, et al., <i>Microbiology, An Amplifiable and Delectable Locus of Streptomyces Ambofaciens RPT81110 Contains a Very Large Gene Homologous to Polyketide Synthase Genes</i> , 142:2815-2824 (1996)
WWM	C2	Aparicio, et al., <i>Gene, Organization of the Biosynthetic Gene Cluster for Rapamycin in Streptomyces Hygroscopicus: Analysis of the Enzymatic Domains in the Modular Polyketide Synthase</i> , 169:9-16 (1996)
WWM	C3	Aparicio, et al., <i>The Journal of Biochemical Chemistry, Limited Proteolysis and Active-Site Studies of the First Multienzyme Component of the Erythromycin-Producing Polyketide Synthase</i> , 269:8524-8528 (1994)
WWM	C4	Ashworth, et al., <i>J. Chem. Soc. Perkin Trans., On the Biosynthetic Origins of the Hydrogen Atoms in the Macrotetrolide Antibiotics: and Their Mode of Assembly Catalysed by a Nonactin Polyketide Synthase</i> , I:1461-1467 (1989)
WWM	C5	Baltz, et al., <i>Ann. Rev. Microbiol., Genetics of Streptomyces Fradiae and Tylosin Biosynthesis</i> , 42:547-574 (1988)
WWM	C6	Bibb, et al., <i>The EMBO Journal, Analysis of the Nucleotide Sequence of the Streptomyces Glaucescens tcml Genes Provides Key Information about the Enzymology of Polyketide Antibiotic Biosynthesis</i> , 8:2727-2736 (1989)

EXAMINER

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SHEET 2 OF 7

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U.S. PATENT DOCUMENTS

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WWM	A7	5,141,926	08-25-92	Weber, et al.	514	29	
WWM	A8	5,252,474	10-12-93	Gerwain, et al.	435	91.1	
WWM	A9	5,672,491	09-30-97	Khosla, et al.	435	148	
WWM	A10	5,712,146	01-27-98	Khosla, et al.	435	252.35	
WWM	A11	5,744,350	04-28-98	Vinci, et al.	435	254.11	
WWM	A12	5,801,032	09-01-98	Stassi, et al.	435	6	

FOREIGN PATENT OR PUBLISHED FOREIGN PATENT APPLICATION

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							YES		
WWM	B5	WO 97/06266	02-20-97	WIPO	—	—			
WWM	B6	WO 97/02358	01-23-97	WIPO	—	—			
WWM	B7	WO 98/01546	01-15-98	WIPO	—	—			
WWM	B8	WO 98/01571	01-15-98	WIPO	—	—			

OTHER DOCUMENTS (Including Author, Title, Date, Place of Publication)

WWM	C7	Brown, et al., <i>J. Chem. Soc. Chem. Commun.</i> , <i>A Mutant Generated by Expression of an Engineered DEB1 Protein from the Erythromycin-Producing Polyketide Synthase (PKS) in Streptomyces Coelicolor Produces the Triketide as a Lactone, but the Major Product is the Nor-Analogue Derived from Acetate as Starter Acid</i> , 15:1517-1518 (1995)
WWM	C8	Caffrey, et al., <i>FEBS Letters, Identification of DEBS 1, DEBS 2 and DEBS 3, the Multienzyme Polypeptides of the Erythromycin-Producing Polyketide Synthase from Saccharopolyspora Erythraea</i> , 304:225, 228 (1992)
WWM	C9	Cane, et al., <i>American Chemical Society, Macrolide Biosynthesis 4 Intact Incorporation of a Chain-Elongation Intermediate into Erythromycin</i> , 109: 1255-1257 (1987)
WWM	C10	Cortes, et al., <i>Nature, An Unusually Large Multifunctional Polypeptide in the Erythromycin-Producing Polyketide Synthase of Saccharopolyspora Erythraea</i> , 348:176-178 (1990)
WWM	C11	Cortes, et al., <i>Nature, Repositioning of a Domain in a Modular Polyketide Synthase to Promote Specific Chain Cleavage</i> , 268:1487-1490 (1995)

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DATE CONSIDERED

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SHEET 3 OF 7

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							YES NO

OTHER DOCUMENTS (Including Author, Title, Date, Place of Publication)

WJM	C12	Dhillon, et al., <i>Molecular Microbiology, Molecular Characterization of a Gene from Saccharopolyspora-Erythraea (Streptomyces-Erythraeus) which is Involved in Erythromycin Biosynthesis</i> , 3(10):1405-1414 (1989)
WJM	C13	Donadio, et al., <i>Gene, Organization of the Enzymatic Domains in the Multifunctional Polyketide Synthase Involved in Erythromycin Formation in Saccharopolyspora Erythraea</i> , 111:51-60 (1992)
WJM	C14	Donadio, et al., <i>Gene, Biosynthesis of the Erythromycin Macrolactone and a Rational Approach for Producing Hybrid Macrolides</i> , 115:97-103 (1992)
WJM	C15	Donadio, et al., <i>Science, Modular Organization of Genes Required for Complex Polyketide Biosynthesis</i> , 252:675-679 (1991)
WJM	C16	Donadio, et al., <i>Genetics and Molecular Biology of Industrial Microorganisms, Genetic Studies on Erythromycin Biosynthesis in Saccharopolyspora Erythraea</i> , 53-59 (1989)
WJM	C17	Fernandez-Moreno, et al., <i>The Journal of Biological Chemistry, DNA Sequence and Functions of the actVT Region of the Actinorhodin Biosynthetic Gene Cluster of Streptomyces Coelicolor A3(2)</i> , 269:24854-24863 (1994)
WJM	C18	Han, et al., <i>Microbiology, Cloning and Characterization of Polyketide Synthase Genes for Jadomycin B Biosynthesis in Streptomyces Venezuela ISP5230</i> , 140:3379-3389 (1994)
WJM	C19	Harris, et al., <i>The Practical Approach Series, Protein Purification Methods</i> , 56-67 (1989)
WJM	C20	Haydock, et al., <i>FEBS Letters, Divergent Sequence Motifs Correlated with the Substrate Specificity of (Methyl) Malonyl-CoA: Acyl Carrier Protein Transacylase Domains in Modular Polyketide Synthesis</i> , 374:246-248 (1995)
WJM	C21	Haydock, et al., <i>Mol. Gen. Genet, Cloning and Sequence Analysis of Genes Involved in Erythromycin Biosynthesis in Saccharopolyspora Erythraea: Sequence Similarities Between EryG and a Family of S-Adenosylmethionine-Dependent Methyltransferases</i> , 230:120-128 (1991)
WJM	C22	Hopwood, et al., <i>GIM 90, Hybrid Pathways for the Production of Secondary Metabolites</i> , Vol. 1:259-270 (1990)
WJM	C23	Hopwood, et al., <i>Ann. Rev. Genet., Molecular Genetics of Polyketides and Its Comparison to Fatty Acid Biosynthesis</i> , 24:37-66 (1990)

EXAMINER

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OTHER DOCUMENTS (Including Author, Title, Date, Place of Publication)

Wurm	C24	Hopwood, et al., <i>Nature, Production of Hybrid Antibiotics by Genetic Engineering</i> , 314:642-644 (1985)
WWM	C25	Hu, et al., <i>Microbiology, Repeated Polyketide Synthase Modules Involved in the Biosynthesis of a Heptaene Macrolide by Streptomyces sp.</i> FR-008, 14(1):163-172 (1994)
Wurm	C26	Huber, et al., <i>Antimicrobial Agents and Chemotherapy, Branched-Chain Fatty Acids Produced by Mutants of Streptomyces Fradiae, Putative Precursors of the Lactone Ring of Tylosin</i> , 34:1535-1541 (1990)
WWM	C27	Hutchinson, et al., <i>Annu. Rev. Microbiol., Polyketide Synthase Gene Manipulation: A Structure-Function Approach in Engineering Novel Antibiotics</i> , 49:201-238 (1995)
WWM	C28	Kakinuma, et al., <i>Tetrahedron, Genetic Studies of the Biosynthesis of Kalafungin, a Benzoisochromanequinone Antibiotic</i> , 31:6059-6068 (1991)
WWM	C29	Kao, et al., <i>Science, Engineered Biosynthesis of a Complete Macrolactone in a Heterologous Host</i> , 265:509-512 (1994)
WLM	C30	Kao, et al., <i>J. Am. Chem. Soc., Engineered Biosynthesis of a Triketide Lactone from an Incomplete Modular Polyketide Synthase</i> , 116:11612-11613 (1994)
WLM	C31	Kao, et al., <i>Journal of Am. Chem. Soc., Manipulation of Macrolide Ring Size by Directed Mutagenesis of a Modular Polyketide Synthase</i> , 117:9105-9106 (1995)
WWM	C32	Kao, et al., <i>Biochemistry, Evidence for Two Catalytically Independent Clusters of Active Sites in a Functional Modular Polyketide Synthase</i> , 35:12363-12368 (1996)
WWM	C33	Kim, et al., <i>Journal of Bacteriology, Heterologous Expression of an Engineered Biosynthetic Pathway: Functional Dissection of Type II Polyketide Synthase Components in Streptomyces Species</i> , 177:1202-1207 (1995)
WLM	C34	Kinoshita, et al., <i>J. Chem. Soc. Chem. Commun., Isolation of Proposed Intermediates in the Biosynthesis of Mycinamicins</i> , 943-945 (1988)
WLM	C35	Kirst, et al., <i>Antimicrobial Agents and Chemotherapy, New Directions for Macrolide Antibiotics: Structural Modifications and in Vitro Activity</i> , 33:1413-1418 (1989)

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OTHER DOCUMENTS (Including Author, Title, Date, Place of Publication)

WWM	C36	Kuhstoss, et al., <i>Gene, Production of a Novel Polyketide Through the Construction of a Hybrid Polyketide Synthase</i> , 183:231-236 (1996)
WWM	C37	Leadlay, et al., <i>Biochemical Society Transactions, The Erythromycin-Producing Polyketide Synthase</i> , 21:218-221 (1993)
WWM	C38	Li, et al., <i>Chinese Journal of Biotechnology, Cloning and Expression of Spiramycin Polyketide Synthase Genes and Resistance Genes from S. Spiramyceticus U-1941</i> , 7:33-42
WWM	C39	MacNeil, et al., <i>Annals of the New York Academy of Sciences, Correlation of the Avermectin Polyketide Synthase Genes to the Avermectin Structure</i> , 721:123-132 (1994)
WWM	C40	Malpartida, et al., <i>Nature, Homology between Streptomyces Genes Coding for Synthesis of Different Polyketides Used to Clone Antibiotic Biosynthetic Genes</i> , 325:818-821 (1987)
WWM	C41	Marsden, et al., <i>Science, Stereospecific Acyl Transfers on the Erythromycin-Producing Polyketide Synthase</i> , 263:378-380 (1994)
WWM	C42	Motamedi, et al., <i>Euro. J. Biochem., Structural Organization of a Multifunctional Polyketide Synthase Involved in the Biosynthesis of the Macrolide Immunosuppressant FK506</i> , 244:74-80 (1997)
WWM	C43	Motamedi, et al., <i>Merck Research Laboratories, FK506 Polyketide Synthase is a Large Multifunctional Polypeptide with 19 FAS-like Domains</i>
WWM	C44	Oliynyk, et al., <i>Chemistry & Biology, A Hybrid Modular Polyketide Synthase Obtained by Domain Swapping</i> , 3:833-839 (1996)
WWM	C45	Omura, et al., <i>J. Antibiotics, Biosynthetic Origin of Carbons 3 and 4 of Leucomycin Aglycone</i> , 36:611-613 (1983)
WWM	C46	Otten, et al., <i>Journal of Bacteriology, Cloning and Expression of Daunorubicin Biosynthesis Genes From Streptomyces Peucetius and S. Peucetius Subsp. Caesius</i> , 172:3427-3434 (1990)
WWM	C47	Pieper, et al., <i>Nature, Cell-Free Synthesis of Polyketides by Recombinant Erythromycin Polyketide Synthases</i> , 378:263-266 (1995)
WWM	C48	Richardson, et al., <i>Journal of Bacteriology, Cloning of Spiramycin Biosynthetic Genes and Their Use in Constructing Streptomyces Ambofaciens Mutants Defective in Spiramycin Biosynthesis</i> , 173:3790-3798 (1990)

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INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Use several sheets if necessary)		APPLICANT(S) L. Katz, et al.	FILING DATE December 11, 2000
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U.S. PATENT DOCUMENTS

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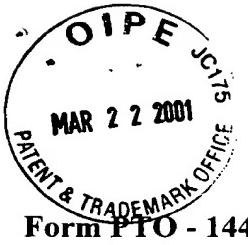
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						YES NO

OTHER DOCUMENTS (Including Author, Title, Date, Place of Publication)

WWM	C49	Robinson, <u>Philosophical Transactions of the Royal Society of London, Polyketide Synthase Complexes: Their Structure and Function in Antibiotic Biosynthesis</u> , 332:107-114
WWM	C50	Salas, et al., <u>BIOTEC-90, Genetic Manipulation of Antibiotic Biosynthesis by Actinomycetes</u> , 47:52 (1990)
WWM	C51	Schwecke, et al., <u>Proc. Natl. Acad. Sci., The Biosynthetic Gene Cluster for the Polyketide Immunosuppressant Rapamycin</u> , 92:7839-7843 (1995)
WWM	C52	Sherman, et al., <u>The EMBO Journal, Structure and Deduced Function of the Granaticin-Producing Polyketide Synthase Gene Cluster of Streptomyces Violaceoruber Tu22</u> , 8:2717-2725 (1989)
WWM	C53	Stanzak, et al., <u>BIO/Technology, Cloning and Expression in Streptomyces Lividans of Clustered Erythromycin Biosynthesis Genes from Streptomyces Erythreus</u> , 4:229-232 (1986)
WWM	C54	Stassi, et al., <u>Journal of Bacteriology, Identification of a Saccharopolyspora Erythraea Gene Required for the Final Hydroxylation Step in Erythromycin Biosynthesis</u> , 175:182-189 (1993)
WWM	C55	Staunton, et al., <u>Nature Structural Biology, Evidence for a Double-Helical Structure for Modular Polyketide Synthases</u> , 3:188-192 (1996)
WWM	C56	Summers, et al., <u>Biochemistry, Malonyl-Coenzyme A:Acyl Carrier Protein Acyltransferase of Streptomyces Glaucescens: A Possible Link Between Fatty Acid and Polyketide Biosynthesis</u> , 34:9389-9402 (1995)
WWM	C57	Swan, et al., <u>Mol. Gen Genet, Characterization of a Streptomyces Antibioticus Gene Encoding a Type I Polyketide Synthase which has an Unusual Coding Sequence</u> , 242:358-362 (1994)
WWM	C58	Tomich, <u>Antimicrobial Agents and Chemotherapy, Streptomyces Cloning: Possible Construction of Novel Compounds and Regulation of Antibiotic Biosynthetic Genes</u> , 32:1472-1476 (1988)
WWM	C59	Tuan, et al., <u>Gene, Cloning of Genes Involved in Erythromycin Biosynthesis from Saccharopolyspora Erythraea using a Novel Actinomycete-Escherichia Coli Cosmid</u> , 90:21-29 (1990)
WWM	C60	Vara, et al., <u>Journal of Bacteriology, Cloning of Genes Governing the Deoxysugar Portion of the Erythromycin Biosynthesis Pathway in Saccharopolyspora Erythraea (Streptomyces Erythreus)</u> , 171:5872-5881 (1989)

EXAMINER	DATE CONSIDERED
<i>Michael Moore</i>	<i>28 September 2001</i>

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